510(k) SUBSTANTIAL EQUIVALENCE DETERMINATION
DECISION SUMMARY
ASSAY ONLY TEMPLATE

A. 510(k) Number:

K050367

B. Purpose for Submission:

clearance of a new device

C. Measurand:

Unfractionated heparin

D. Type of Test:

Chromogenic assay

E. Applicant:

Hyphen BioMed

F. Proprietary and Established Names:

Biophen Heparin 6
Biophen Heparin 3

G. Regulatory Information:

1. Regulation section:

21 CFR 864.7525

2. Classification:

Class II

3. Product code:

   KFF

4. Panel:

   81 Hematology

H. Intended Use:

1. Intended use(s):

The Hyphen Biomed Biophen Heparin 6 and Biophen Heparin 3 are chromogenic assays for measuring the quantitative level of unfractionated heparin in human citrated plasma using an automatic or manual method.

2. Indication(s) for use:

   Heparin is used for curative or preventive indications. Measuring heparin concentration in patient's plasma allows monitoring therapy and adjusting drug dosage.

3. Special conditions for use statement(s):

4. Special instrument requirements:

I. Device Description:

The assay kit is available in two sizes and consists of an FXa specific chromogenic substrate (SXa-11), and bovine FXa reagent. The Biophen Heparin 3 is supplied with 3 vials of substrate and 3 vials of Xa reagent. The Biophen Heparin 6 is supplied with 4 vials substrate and 4 vials of Xa reagent.

J. Substantial Equivalence Information:

1. Predicate device name(s):

   1. IL Coamatic® Heparin assay

   2. Diagnostica Stago Rotachrom

2. Predicate 510(k) number(s):

   1. K983178

   2. K010455

3. Comparison with predicate:

Similarities		
Item	Device	Predicate
Intended Use	Quantitative level of unfractionated heparin in human using an automatic or manual method.	same
test principle	chromogenic assay	same
sample requirements	citrated plasma	same

Differences		
Item	Device	Predicate
kit size	Biophen 6- 60 tests Biophen 3- 30 tests	200 microplate determinations per kit

K. Standard/Guidance Document Referenced (if applicable):

L. Test Principle:

The Biophen Heparin assay employs a two stage FXa method for the determination of heparin and low molecular weight (LMW) heparin in plasma. The assay principle is a kinetic method based on the inhibition of a constant amount of factor Xa, by the tested heparin in presence of endogenous antithrombin, and hydrolysis of the Factor Xa specific substrate, by the factor Xs in excess. pNA is then released from the substrate. The released pNA is measured at 405 nm, and is inversely proportional to the heparin level in the test plasma.

M. Performance Characteristics (if/when applicable):

1. Analytical performance:

   a. Precision/Reproducibility:

Intra-assay- 2 calibrators (0.38 IU/ml and 0.74 IU/ml) were assayed a total of 15 times. % CV < 2.10 %.

Inter-assay-a total of 20 samples were assayed a total of 20 times. % CV < 2.4%.

b. *Linearity/assay reportable range:*

c. *Traceability, Stability, Expected values (controls, calibrators, or methods):*

d. *Detection limit:*

e. *Analytical specificity:*

Normal pooled human plasma was spiked with 0, 0.1 µg/ml, and 1 µg/ml of PF4 concentrations, supplemented with UFH (concentrations of 0.2 IU/ml and 0.5 IU/ml) and assayed with Biophen Heparin. Testing demonstrated little interference due to PF4.

ATIII interference testing demonstrated high ATIII concentrations (>150%) can interfere in the Biophen assay.

Bilirubin, hemoglobin, and lipemia inference testing demonstrated no significant interference of bilirubin up to 0.1 mg/ml, hemoglobin up to 2 mg/ml, and lipemia up to 1.25 mg/ml.

f. *Assay cut-off:*

2. <u>Comparison studies:</u>

a. *Method comparison with predicate device:*

Study 1- n= 55. Biophen Heparin compared to predicate 1 on the STA (K983460) (y=0.87x-0.6, r=0.98) and BCS (y=0.91x-0.03, r=0.99) analyzers.

Study 2-n= 131. Biophen Heparin compared to predicate 2 on the STA analyzer (y=1.07x + 0.06, r=0.97).

Study 3- n=40. Biophen Heparin compared to predicate 2 on the STA analyzer (y= 0.93x-0.02, r=0.98).

Studies 1 & 2 were conducted in France, Study 3 in the US.

b. Matrix comparison:

3. Clinical studies:

a. Clinical Sensitivity:

n = 47 (20 normals, 11 patients on AVK therapy, 4 hepatic disease, 12 heparinized). Assay performed on automated (IL ACL7000) and manual method. Normal and hepatic samples contained <0.05 IU/ml heparin, confirming the detection threshold of 0.05 IU/ml.

b. Clinical specificity:

c. Other clinical supportive data (when a. and b. are not applicable):

4. Clinical cut-off:

5. Expected values/Reference range:

N. Proposed Labeling:

The labeling is sufficient and it satisfies the requirements of 21 CFR Part 809.10.

O. Conclusion:

The submitted information in this premarket notification is complete and supports a substantial equivalence decision.